

Shukla, Ram

From: Shukla, Ram
Sent: Monday, April 23, 2001 5:11 PM
To: 'jliebeschuetz@townsend.com'
Subject: RE: 3137117 v1 - draft claims

Mr. Liebeschuetz,

Attached is the draft of claims. Please let me know what you think.

Thanks.



Examlner
Amendment.doc

.....
Ram R. Shukla, Ph.D.
Patent Examiner
AU 1632
Crystal Mall 1, Rm 12E03
USPTO
Phone: (703) 305-1677
Fax : (703) 308-8724

Art Unit: 1632

DRAFT EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Joe Liebeschuetz on -----.

The application has been amended as follows:

IN THE CLAIMS:

Claims 1-21 and 54-88 have been canceled.

New claims 91-¹¹⁶~~142~~ have been added.

-- 91~~147~~. A method of screening a candidate agent for an effect on cell death activity, said method comprising in the following order:

(a) contacting a living teleost post 12-hours of development with a dye wherein said dye has an affinity for dead cells and wherein said dye stains dead cells;

(b) administering the candidate agent to the living teleost;

(c) detecting the staining of dead cells with said dye in at least one specific tissue or organ in the living teleost ;

comparing the staining of dead cells with said dye in said at least one specific tissue or organ of the living teleost with the staining of dead cells with said dye in said at least one specific tissue or organ of a control living teleost that was not administered said candidate agent;

wherein an increase or decrease in the staining of dead cells with said dye in the treated living teleost compared to the control living teleost would indicate the effect of the candidate compound on cell death activity.

92. ~~418~~. The method of claim 91 ~~447~~, wherein the effect is an increase in cell death activity.

93. ~~419~~. The method of claim 92 ~~448~~, wherein the method further comprises detecting a change in cell death activity in the living teleost after a predetermined period of time, wherein

Art Unit: 1632

said predetermined period of time is sufficient for a detectable difference in cell death activity to occur in presence of the candidate agent.

94. 420. The method of claim 93 419, wherein the method further comprises detecting the increase in cell death activity over time at predetermined intervals.

95. 421. The method of claim 92 418, wherein the increase in cell death activity is detected in more than one tissue or organ of the living teleost simultaneously.

96. 422. The method of claim 95 421, wherein the increase in cell death activity is detected in more than one tissue or organ of the living teleost simultaneously over time at predetermined intervals.

97 423. The method of claim 91 417, wherein the effect is a decrease in cell death activity.

98 424. The method of claim 91 417, wherein the effect is an increase in apoptotic activity or necrotic activity.

99 425. The method of claim 98 424, wherein the increase in apoptotic activity comprises an increase in cell death in said at least one specific tissue or organ of the living teleost.

100 426. The method of claim 98 424, wherein the increase in apoptotic activity is detected by light microscopy or fluorescence microscopy.

101 427. The method of claim 98 424, wherein the increase in apoptotic activity or necrotic activity is detected in at least one specific organ or tissue.

102 428. The method of claim 91 417, wherein the effect is a decrease in apoptotic activity or necrotic activity.

Art Unit: 1632

103 429. The method of claim 102 428, wherein the decrease in apoptotic activity comprises a decrease in cell death in said at least one specific tissue or organ of the living teleost.

104 430. The method of claim 91 447, wherein the candidate agent is administered to the living teleost by dissolving the candidate agent in culture media containing the living teleost.

105 431. The method of claim 91 447, wherein a fluorescent dye which labels dead or dying cells is administered to the teleost prior to administration of the candidate agent to the living teleost.

106 432. The method of claim 105 431, wherein the fluorescent dye is administered to the living teleost by dissolving the fluorescent dye in media containing the living teleost.

107 433. The method of claim 105 431, wherein the fluorescent dye is administered to the living teleost by injecting the fluorescent dye into the living teleost.

108 434. The method of claim 105 431, further comprising administering the candidate agent to the living teleost by dissolving the candidate agent in the culture media containing the living teleost or injecting the candidate agent into the living teleost after administration of the fluorescent dye to the living teleost.

109 435. The method of claim 105 431, wherein a fluorescent dye is a monomeric cyanine dye.

110 436. The method of claim 109 435, wherein the fluorescent dye is benzothiazolium-4-quinolium dye.

111 437. The method of claim 91 447, wherein the living teleost is a zebrafish.

112 438. The method of claim 91 447, wherein the candidate agent is a compound and a library of compounds is screened for an effect on cell death activity.

Art Unit: 1632

113 439. The method of claim 91 447, further comprising screening the candidate agent for a toxic activity.

114 440. The method of claim 91 447, wherein the method is conducted in a living teleost in vivo.

115 441. The method of claim 91 447, wherein the living teleost is contained in a microtiter well.

116 442. The method of claim 91 447, wherein the dye in said at least one specific tissue or organ is detected using a microplate reader. –

2. The following is an examiner's statement of reasons for allowance:

The claimed invention is free of the prior art of record the prior art of record does not teach or fairly suggest using a living teleost post 12 hours of development in screening for candidate agents that alter cell death activity, wherein a dye to stain dead cells is contacted to the living teleost before the candidate agents are administered to the living teleost .

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Kay Pinkney whose telephone number is (703) 305-3553.

Application/Control Number: 09/255,397

Art Unit: 1632

Page 6

Ram R. Shukla, Ph.D.